

WHAT IS CLAIMED IS:

1. An isolated variant allele of a human mu opioid receptor gene, comprising a DNA sequence having a variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.
2. The isolated variant allele of Claim 1, detectably labeled.
3. The isolated variant allele of Claim 2, wherein said detectable label comprises a radioactive element, a chemical which fluoresces, or an enzyme.
4. An isolated nucleic acid molecule selectively hybridizable to the isolated variant allele of Claim 1.
5. The isolated nucleic acid molecule of Claim 4, detectably labeled.
6. The isolated nucleic acid molecule of Claim 5, wherein said detectable label comprises a radioactive element, a chemical that fluoresces, or an enzyme.
7. An isolated variant allele of a human mu opioid receptor gene which encodes a variant human mu opioid receptor comprising an amino acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63.
8. An isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of Claim 1, wherein said isolated nucleic acid molecule encodes a variant human mu opioid receptor comprising an amino acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63.
9. A isolated variant human mu opioid receptor comprising an amino acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro,

Ser42Thr or the addition of a Gly residue following Gly 63.

10. An antibody having a variant human mu opioid receptor of Claim 9 as an immunogen.
11. The antibody of Claim 10, which is a polyclonal antibody.
12. The antibody of Claim 10, which is a monoclonal antibody.
13. The antibody of Claim 10, which is a chimeric antibody.
14. The antibody of Claim 10, detectably labeled
15. The antibody of Claim 14, wherein said detectable label comprises a radioactive element, a chemical that fluoresces, or an enzyme.
16. A cloning vector comprising an isolated variant allele of a human mu opioid receptor gene and an origin of replication, wherein said variant allele comprises a DNA sequence having a variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.
17. A cloning vector comprising an origin of replication and an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said variant allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.
18. The cloning vector of either of Claims 16 or 17, wherein said cloning vector comprises of *E. coli*, bacteriophages, plasmids, or pUC plasmid derivatives.
19. The cloning vector of Claim 18, wherein bacteriophages further comprise lambda derivatives, plasmids further comprise pBR322 derivatives, and pUC plasmid

derivatives further comprise pGEX vectors, or pmal-c, pFLAG.

20. An expression vector comprising an isolated variant allele of a human mu opioid receptor gene comprising a DNA sequence having a variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.
21. An expression vector comprising an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and said variant allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.
22. The expression vector of either of Claims 20 or 21, wherein said promoter comprises immediate early promoters of hCMV, early promoters of SV40, early promoters of adenovirus, early promoters of vaccinia, early promoters of polyoma, late promoters of SV40, late promoters of adenovirus, late promoters of vaccinia, late promoters of polyoma, the *lac* the *trp* system, the *TAC* system, the *TRC* system, the major operator and promoter regions of phage lambda, control regions of fd coat protein, 3-phosphoglycerate kinase promoter, acid phosphatase promoter, or promoters of yeast α mating factor.
23. A unicellular host transformed or transfected with an expression vector comprising an isolated variant allele of a human mu opioid receptor gene operatively associated with a promoter, wherein said variant allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.
24. A unicellular host transformed with an expression vector comprising an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu

1 opioid receptor gene, wherein said isolated nucleic acid molecule is operatively
2 associated with a promoter, and said variant allele comprises a DNA sequence having
3 at least one variation in SEQ ID NO:1, wherein said at least one variation comprises
4 T67C, T124A; C153T; G174A or 187INS:GGC, or combinations thereof.

5
6 25. The unicellular host of either of Claims 23 or 24, wherein said host comprises *E. coli*,
7 *Pseudomonas*, *Bacillus*, *Streptomyces*, yeast, CHO, R1.1, B-W, L-M, COS1, COS7,
8 BSC1, BSC40, BMT10 or Sf9 cells.

9
10 26. A method of producing an a variant human mu opioid receptor comprising an amino
11 acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises
12 Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63, said method
13 comprising the steps of:

- 14 a) culturing a unicellular host of either of Claims 23 or 24 under conditions that
15 provide for expression of said variant human mu opioid receptor; and
16 b) recovering said variant human mu opioid receptor from said unicellular host.

17
18 27. An isolated variant allele of a human mu opioid receptor gene, wherein said variant
19 allele comprises a DNA sequence having at least two variations in SEQ ID NO:1,
20 wherein said variations comprise T67C; T124A; C153T; G174A or 187INS:GGC, .

21
22 28. The isolated variant allele of Claim 27, detectably labeled.

23
24 29. The isolated variant allele of Claim 28, wherein said detectable label comprises a
25 radioactive element, a chemical that fluoresces, or an enzyme.

26
27 30. An isolated nucleic acid molecule selectively hybridizable to an isolated variant allele
28 of a human mu opioid receptor gene comprising a DNA sequence having at least two
29 variations in SEQ ID NO:1, wherein at least one of said variations comprises T67C;
30 T124A; C153T; G174A or 187INS:GGC.

1 said isolated nucleic acid molecule is operatively associated with a promoter, and said
2 variant allele comprises a DNA sequence having at least two variations in SEQ ID
3 NO:1, wherein at least one of said variations comprises T67C; T124A; C153T;
4 G174A; or 187INS:GGC.

5
6 48. The expression vector of either of Claims 46 or 47, wherein said promoter comprises
7 immediate early promoters of hCMV, early promoters of SV40, early promoters of
8 adenovirus, early promoters of vaccinia, early promoters of polyoma, late promoters of
9 SV40, late promoters of adenovirus, late promoters of vaccinia, late promoters of
10 polyoma, the *lac* the *trp* system, the *TAC* system, the *TRC* system, the major operator
11 and promoter regions of phage lambda, control regions of fd coat protein, 3-
12 phosphoglycerate kinase promoter, acid phosphatase promoter, or promoters of yeast α
13 mating factor.

14
15 49. A unicellular host transformed with an expression vector of Claim 46.

16
17 50. A unicellular host transformed with an expression vector of Claim 47.

18
19 51. The unicellular host of either of Claims 49 or 50, wherein said host comprises *E. coli*,
20 *Pseudomonas*, *Bacillus*, *Streptomyces*, yeast, CHO, R1.1, B-W, L-M, COS1, COS7,
21 BSC1, BSC40, BMT10 or Sf9 cells.

22
23 52. A method for producing a variant human mu opioid receptor comprising an amino acid
24 sequence having at least two variations in SEQ ID NO:2, wherein at least one of said
25 variations comprises Ser23Pro, Ser42Thr; or the addition of a Gly residue following
26 Gly63, wherein the method comprising the steps of:

- 27 a) culturing a unicellular host of either of Claims 49 or 50 under
28 conditions that provide for expression of said variant human mu opioid
29 receptor; and
30 b) recovering said variant human mu opioid receptor from said unicellular
31 host.

- 1 53. A method for determining a susceptibility in a subject to at least one addictive disease,
2 comprising the steps of:
- 3 a) removing a bodily sample from said subject, wherein said sample comprises a
4 first and second allele comprising a human mu opioid receptor gene;
- 5 b) determining whether said human mu opioid receptor gene of said first allele
6 comprises a DNA sequence having at least one variation in SEQ ID NO:1,
7 wherein said variation comprises T67C; T124A; or 187INS:GGC,
8 such that the presence of said at least one variation in said human mu opioid receptor
9 gene of said first allele is expected to be indicative of the subject's susceptibility to at
10 least one addictive disease relative to the susceptibility to said at least one addictive
11 disease in a standard.
- 12
- 13 54. The method for determining a susceptibility to at least one addictive disease of Claim
14 53, further comprising the step of determining whether said human mu opioid receptor
15 gene of said second allele comprises a DNA sequence having at least one variation in
16 SEQ ID NO:1, wherein said variation comprises T67C; T124A; or
17 187INS:GGC, such that the presence of said at least one variation in said human mu
18 opioid receptor gene of said second allele is expected to be indicative of the subject's
19 susceptibility to said at least one addictive disease relative to the susceptibility to said at
20 least one addictive disease in said standard.
- 21
- 22 55. The method of either of Claim 54 wherein said at least one addictive disease comprises
23 opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine
24 addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or
25 alcohol addiction.
- 26
- 27 56. The method of Claim 55, wherein said at least addictive disease comprises opioid
28 addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction;
29 barbituate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.
- 30
- 31 57. A method for determining a susceptibility to at least one addictive disease in a subject

relative to susceptibility in a standard, comprising the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a human mu opioid receptor;
- b) determining whether said human mu opioid receptor comprises an amino acid sequence having at least one variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro, Ser42Thr; or addition of a Gly residue following Gly63, such that the presence of said at least one variation is expected to be indicative of the susceptibility to said at least one addictive disease in said subject relative to susceptibility to said at least one addictive disease in said standard, wherein the human mu opioid receptor of said standard comprises an amino acid sequence of SEQ ID NO:2.

58. The method of Claim 57, wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.

59. A method for determining a susceptibility to pain in a subject relative to a susceptibility of pain in a standard, wherein the method comprises the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene;
- b) determining whether said human mu opioid receptor gene of said first allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC,

such that the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

60. The method of Claim 59 for determining a susceptibility to pain in a subject, further

1 comprising the step of determining whether said second allele of said bodily sample
2 comprises a human mu opioid receptor gene comprising a DNA sequence having at
3 least one variation in SEQ ID NO:1, wherein said variation comprises T67C, T124A
4 or 187INS:GGC, such that the presence of said at least one variation in said second
5 allele is expected to be indicative of susceptibility to pain in said subject relative to
6 susceptibility of pain in said standard, wherein said second allele of said standard
7 comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID
8 NO:1.

9
10 61. A method for determining a therapeutically effective amount of pain reliever to
11 administer to a subject in order to induce analgesia in said subject relative to a
12 therapeutically effective amount of pain reliever to administer to a standard in order to
13 induce analgesia in said standard, wherein the method comprises determining a
14 susceptibility to pain in said subject relative to susceptibility to pain in said standard,
15 wherein susceptibility to pain in said subject is expected to be indicative of said
16 therapeutically effective amount of pain reliever to administer to said subject to induce
17 analgesia in said subject relative to said therapeutically effective amount of pain
18 reliever to administer to said standard to induce analgesia in said standard.

19
20 62. The method of Claim 61 for determining a therapeutically effective amount of pain
21 reliever to administer to said subject, wherein determining susceptibility to pain in said
22 subject comprises the steps of:

- 23 a) removing a bodily sample from said subject, wherein said sample comprises a
24 first and second allele comprising a human mu opioid receptor gene; and
25 b) determining whether said first allele comprises a human mu opioid receptor
26 gene comprising a DNA sequence having at least one variation in SEQ ID
27 NO:1, wherein said at least one variation comprises T67C, T124A or
28 187INS:GGC,

29 wherein the presence of said at least one variation in said human mu opioid receptor
30 gene of said first allele is expected to be indicative of the subject's susceptibility to pain
31 relative to said to susceptibility of pain in said standard, wherein said first allele of said

standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, such that said therapeutically effective amount of pain reliever to administer to the subject in order to induce analgesia is related to said susceptibility to pain in said subject relative to susceptibility to pain in said standard.

63. The method of Claim 62, wherein determining susceptibility to pain in said subject relative to susceptibility to pain in said standard further comprises the step of determining whether said second allele of said bodily sample from said subject comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises T67C, T124A or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, and the therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject is related to the presence of said at least one variation in said human mu opioid receptor gene of said second allele of said bodily sample from said subject.

64. A method for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from at least one addictive disease to treat the at least one addictive disease in said subject relative to a therapeutically effective amount of therapeutic agent to administer to a standard suffering from the at least one addictive disease to treat the at least one addictive disease in said standard, wherein the method comprises the steps of:

- a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene; and
- b) determining whether said first allele comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C, T124A or 187INS:GGC, wherein the presence of said at least one variation in said human mu opioid receptor

1 gene of said first allele is expected to be indicative of the therapeutically effective
2 amount of said therapeutic agent to administer to the subject to treat said at least one
3 addictive disease in said subject relative to said therapeutically effective amount of said
4 therapeutic agent to administer to said standard to treat said at least one addictive
5 disease in said standard, wherein said first allele of said standard comprises a human
6 mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

7
8 65. The method of Claim 64 for determining a therapeutically effective amount of
9 therapeutic agent to administer to a subject suffering from said at least one addictive
10 disease to treat said at least one addictive disease, relative to said therapeutically
11 effective amount of said therapeutic agent administered to said standard suffering from
12 said at least one addictive disease to treat said at least one addictive disease in said
13 standard, further comprising the step of determining whether said second allele of said
14 bodily sample from said subject comprises a human mu opioid receptor gene
15 comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein
16 said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of
17 said at least one variation in said second allele related to said therapeutically effective
18 amount of said therapeutic agent administered to said subject to treat said at least one
19 addictive disease in said subject relative to said therapeutically effective amount of said
20 therapeutic agent to administer to said standard to treat said at least one addictive
21 disease in said standard, wherein said second allele of said standard comprises a human
22 mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

23
24 66. The method of either of Claims 64 or 65, wherein said at least one addictive disease
25 comprises opioid addiction; cocaine addiction or addiction to other psychostimulants;
26 nicotine addiction; barbiturate or sedative hypnotic addiction; anxiolytic addiction; or
27 alcohol addiction.

28
29 67. A commercial test kit may for determining the presence of at least one variation in a
30 human mu opioid receptor gene of an allele in a bodily sample taken from a subject,
31 wherein the commercial test kit comprises:

- 1 a) PCR oligonucleotide primers suitable for detection of an allele comprising a
2 human mu opioid receptor gene comprising a DNA sequence having at least
3 one variation in SEQ ID NO:1 comprising T67C; T124A; C153T; G174A; or
4 187INS:GGC;
5 b) other reagents; and
6 c) directions for use of the kit.

7
8 68. A commercial test kit for detecting a variant human mu opioid receptor in a bodily
9 sample taken from a subject, comprising

- 10 (a) predetermined amount of at least one detectably labeled immunochemically
11 reactive component having affinity for a variant human mu opioid receptor;
12 said variant being at least one of T67C; T124A; C153T; G174A; or
13 187INS:GGC.
14 (b) other reagents; and
15 (c) directions for use of the kit.

16
17 69. A commercial test kit for detecting a variant human mu opioid receptor in a bodily
18 sample taken from a subject, wherein said kit comprises:

- 19 (a) a labeled component which has been obtained by coupling the human mu
20 opioid receptor of the bodily sample to a detectable label;
21 (b) one or more additional immunochemical reagents of which at least one reagent
22 is a ligand or an immobilized ligand, which ligand comprises:
23 (i) a ligand capable of binding with the labeled component (a);
24 (ii) a ligand capable of binding with a binding partner of the labeled
25 component (a);
26 (iii) a ligand capable of binding with at least one of the component(s) to be
27 determined; or
28 (iv) a ligand capable of binding with at least one of the binding partners of
29 at least one of the component(s) to be determined;
30 (c) directions for the performance of a protocol for the detection and/or
31 determination of one or more components of an immunochemical reaction

1 between the human mu opioid receptor and a specific binding partner thereto.

- 2
- 3 70. A method for diagnosing a disease or disorder related to a physiological function
- 4 regulated by the hypothalamus pituitary adrenal axis (HPA) or the hypothalamus
- 5 pituitary gonadal axis (HPG), wherein the method comprises the steps of:
- 6 a) removing a bodily sample from said subject, wherein said sample comprises a
- 7 first and second allele comprising a human mu opioid receptor gene;
- 8 b) determining whether said human mu opioid receptor gene of said first allele
- 9 comprises a DNA sequence having at least one variation in SEQ ID NO:1,
- 10 wherein said variation comprises T67C; T124A; or 187INS:GGC,
- 11 such that the presence of said at least one variation in said human mu opioid receptor
- 12 gene of said first allele is expected to be indicative of a disease or disorder related to a
- 13 physiological function regulated by the hypothalamus pituitary adrenal axis (HPA) or
- 14 the hypothalamus pituitary gonadal axis (HPG), wherein said first allele of said
- 15 standard comprises a human mu opioid receptor gene comprising a DNA sequence of
- 16 SEQ ID NO:1.
- 17
- 18 71. The method of Claim 70, wherein said physiological function comprises sexual or
- 19 reproductive function, gastrointestinal motility, immune response, or ability to
- 20 withstand stress.
- 21
- 22 72. The method of Claim 71, wherein said disease or disorder comprises infertility,
- 23 constipation, diarrhea, decreased immune response relative to said standard, or
- 24 decreased ability to withstand stress relative to said standard.
- 25
- 26 73. The method of Claim 70 for diagnosing a disease or disorder related to a physiological
- 27 function regulated by the HPA or HPG, further comprising the step of determining
- 28 whether said second allele of said bodily sample comprises a human mu opioid receptor
- 29 gene comprising a DNA sequence having at least one variation in SEQ ID NO:1,
- 30 wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the
- 31 presence of said at least one variation in said second allele is expected to be indicative

1 of a disease or disorder related to a physiological function regulated by the HPA or
2 HPG axes, wherein said second allele of said standard comprises a human mu opioid
3 receptor gene comprising a DNA sequence of SEQ ID NO:1.

4
5 74. The method of Claim 73, wherein said physiological function comprises sexual or
6 reproductive function, gastrointestinal motility, immune response, or ability to
7 withstand stress.

8
9 75. The method of Claim 73, wherein said disease or disorder comprises infertility,
10 constipation, diarrhea, decreased immune response relative to said standard, or
11 decreased ability to withstand stress relative to said standard.

12
13 76. The method of Claim 76, wherein said disease or disorder comprises diarrhea.

14
15 77. A method for selecting an appropriate therapeutic agent and a therapeutically effective
16 amount of said agent to administer to said subject to treating a disease or disorder
17 related to a physiological function regulated by the HPA or HPG axes, wherein the
18 method comprises diagnosing said disease or disorder in said subject, wherein said
19 disease or disorder is expected to be indicative of said appropriate therapeutic agent for
20 treating said disease or disorder.

21
22 78. The method of Claim 77, wherein said physiological function comprises reproductive
23 or sexual function, gastrointestinal motility, immune response, or ability to withstand
24 stress.

25
26 79. The method of Claim 78, wherein diagnosing said disease or disorder in said subject
27 comprises the steps of:

- 28 a) removing a bodily sample from said subject, wherein said sample comprises a
29 first and second allele comprising a human mu opioid receptor gene; and
30 b) determining whether said first allele comprises a human mu opioid receptor
31 gene comprising a DNA sequence having at least one variation in SEQ ID

1 NO:1, wherein said at least one variation comprises T67C; T124A; or
2 187INS:GGC,

3 wherein the presence of said at least one variation in said human mu opioid receptor
4 gene of said first allele is expected to be indicative of said disease or disorder related to
5 a physiological function regulated by the HPA or HPG axes.
6

7 80. The method of Claim 79, wherein diagnosing a disease or disorder related to a
8 physiological function regulated by the HPA or HPG further comprises the step of
9 determining whether said second allele of said bodily sample comprises a human mu
10 opioid receptor gene comprising a DNA sequence having at least one variation in SEQ
11 ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that
12 the presence of said at least one variation in said second allele is expected to be
13 indicative of a disease or disorder related to a physiological function regulated by the
14 HPA or HPG axes, wherein said second allele of said standard comprises a human mu
15 opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.
16

17 81. The method of Claim 80, wherein said physiological function comprises reproductive
18 or sexual function, gastrointestinal motility, immune response, or ability to withstand
19 stress.
20

21 82. The method of Claim 80, wherein said disease or disorder comprises infertility,
22 constipation, diarrhea, decreased immune response relative to immune response in said
23 standard, or decreased ability to withstand stress relative to ability to withstand stress
24 of said standard.
25

26 83. The method of Claim 82, wherein said disease or disorder comprises diarrhea.
27
28